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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/848,866	05/04/2001	Duncan McRee	22700-706	8379
32793	7590	10/31/2005		
TAKEDA SAN DIEGO, INC. 10410 SCIENCE CENTER DRIVE SAN DIEGO, CA 92121				
			EXAMINER BORIN, MICHAEL L	
			ART UNIT	PAPER NUMBER
			1631	

DATE MAILED: 10/31/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/848,866

Applicant(s)

MCREE ET AL.

Examiner

Michael Borin

Art Unit

1631

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on 19 August 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☐ Claim(s) 1-57 is/are pending in the application.

4a) Of the above claim(s) 8-12, 15, 17-20, 27-30, 37, 39, 41, 43, 44, 46, 47 and 49-51 is/are withdrawn from consideration.

- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-7, 16, 21-26, 31-36, 38, 40, 42, 45, 48 and 52-57 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 10/07/2005.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 08/19/2005 has been entered.

Status of Claims

Claims 1-57 are pending. Claims 8-12,15,17-20,27-30,37,39, 41,43, 44,46, 47,49-51 remain withdrawn from consideration as drawn to non-elected species. Claims 1-7,16,21-26,31-36,38,40,42,45,48,52-57 are under examination.

Applicant amended independent claims 1,52-57 to limit the claims to non-iterative fashion of conducting the first step of the method, performing multiple replacement searches, and second step, comparing the results of the first step to identify search model for use in molecular replacement to determine target molecule's structure. Consequently, the following rejections are deemed necessary.

Claim Rejections - 35 USC § 112, first paragraph (written description)

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-7,16,21-26,31-36,38,40,42,45,48-57 are rejected under 35

U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

The independent claims 1,52-57 are amended to recite "non-iterative manner" of performing first step and second steps of the method. The "non-iterative manner" is a new matter not disclosed in the specification as filed. Contrary, specification describes iterative manner of identifying search models- see p. 43, lines 10-18, for example.

Claim Rejections - 35 USC § 103.

Claims 1-7,16,21-26,31-36,38,40,42,45,48-57 are rejected under 35 U.S.C. 103(a) as obvious over Kissinger et al. (Acta Crystallographica Section D, Biological Crystallography, 1999, D55, 484-491).

The instant claims are drawn to method for identifying a search model to use in molecular replacement for determining a structure of a target biomolecule from crystal data, the method comprising:

employing computer executable logic to perform multiple molecular replacement searches on crystal data of the target biomolecule where a group of structures of different biomolecules are used as search models for the multiple molecular replacement searches; and

employing computer executable logic in non-iterative manner relative to the operation of the first step to compare solutions from the multiple molecular replacement searches, the comparison producing data from which biomolecule

structures in the group can be identified as having superior structural identity with the target biomolecule as compared to the other biomolecule structures in the group.

Kissinger teaches method of automated molecular replacement by evolutionary search, EPMR. Note, that EPMR is the preferred method of performing molecular replacement search in the instant invention (see pages 27,35). The referenced method is a computerized method of molecular replacement wherein the target structure is determined using a search model. A population of initially random molecular-replacement solutions is generated for a given biomolecule and structure factors are calculated for each solution (*compare to the first step of the instant method*). Then, the solutions are ranked, compared, and the survivors are selected (*compare to the second step of the instant invention*). See pages 485-486 and Figure 1. The referenced method uses statistical analysis to identify validity of molecular replacement solution. The method can utilize either single or multiple molecules (see paragraph bridging columns on p. 490).

Unlike the instant method, Kissinger reference does not teach use of a group of biomolecules for multiple searches at once. However, the reference clearly addresses such parallel approach of using multiple search models as one of potential enhancement of EPMR method. Thus, on p. 490 (right column, first full paragraph) Kissinger discusses that simultaneous searches for multiple molecules or domains could be a useful approach instead of a single search model.

It would be *prima facie* obvious to substitute single search model method of molecular replacement with using multiple search models and multiple molecular replacements because Kissinger teaches that using multiple search models will enhance the applicability of the MR method and will enhance the search efficiency. One

would expect that the possibility of success in utilizing multiple search models in the method of Kissinger will be at least as effective as the use of single search model.

With respect to the amended claim language specifying that molecular searches and their comparison are done in non-iterative manner, these steps are non conducted in the iterative manner in the reference either. The whole process of molecular replacement can be repeated (iterated) after random alterations to survived best solutions are made (see Figure 1, step 5), and method iterated; however, the instant method has open "comprising" language which does not exclude such additional steps.

With respect to claims 53-55, it would be obvious that the selection of different structures should continue will continue until a molecular replacement is produced, and then to use such molecular replacement to identify the structure of the target molecule - the latter being the final objective of any method of molecular replacement.

Further, with respect to dependent claims addressing particular criteria of selecting structures, conducting the method, and comparing the degree of similarity of structures, the reference does not expressly teach these criteria, as it is drawn to use of single model, rather than plurality of models. Absent some teaching to the contrary however, the determination of such criteria is within the skill of the ordinary worker as a part of the process of normal optimization. Applicant's claims are directed to optimization of an "art recognized variables" which is well within the perview of one of ordinary skill in the art. In re Boesch, 617 F. 2d 272, 205 USPQ 215 (CCPA 1980).

Response to arguments

Applicant argues that Kissinger does not teach how multiple search models would "compete". First, the lack of such clear description does not remove the suggestion in the reference to use multiple molecular replacement searches. Second,

by "competing" the reference understands rank ordering of candidates by their scoring and discarding lower scoring individuals, i.e., the same method steps as in the instant method.

Further, applicant argues that Kissinger process optimizes search parameters only for the selected search model. This is not correct. The reference both teaches that the method can utilize either single or multiple molecules (see paragraph bridging columns on p. 490) and suggests that instead of single search model, a set of structural models can be used (p. 490, last paragraph).

Further, applicant argues that, unlike the Kissinger process searching for the best optimal conditions, the instant method only "provides a basis for comparing search models". First, the same is achieved by the Kissinger method, which comprises the steps of the instant method, but proceeds further in repeating them for another set of models. Second, it was Examiner's understanding that the objective of the instant method is not providing a "basis for comparing search models" , but rather "identifying a search model" (i.e., as per claim 1).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Borin whose telephone number is (571) 272-0713. The examiner can normally be reached on 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, Ph.D., can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Michael Borin, Ph.D.
Primary Examiner
Art Unit 1631

mlb
10/25/2005